

**REMARKS**

Reconsideration and withdrawal of the rejections of this application and consideration and entry of this paper are respectfully requested in view of the herein amendment and remarks, which place the application in condition for allowance.

The Examiner is thanked for indicating that the rejections under 35 U.S.C. §§ 102 and 103, and the previous rejection under 35 U.S.C. § 112, first paragraph regarding new matter, have all been withdrawn.

**I. STATUS OF CLAIMS AND FORMAL MATTERS**

Claims 1, 18, 29, 31, and 37 are currently under consideration. Claims 1, 18, 29, and 31 are amended, claim 2 is newly cancelled, and claim 37 is newly added without prejudice, without admission, without surrender of subject matter and without intention of creating any estoppel as to equivalents.

Support for the amendments can be found throughout the specification as originally filed. For instance, the amendment of claim 1 can be found, as an example, on page 3, lines 27-32, on page 4, lines 1-17, on page 6, lines 6-24, and in original claim 2. Support for new claim 37 can be found, for example, on page 3, lines 27-32, on page 4, lines 1-17, on page 5, line 33 - page 6, line 4, on page 13, lines 5-10, on page 47, line 23 - page 48, line 24, and in claim 1 as previously pending. The amendments to claims 18, 29, and 31 are to perfect antecedent basis. No new matter is added.

It is respectfully submitted that the claims, herewith and as originally presented, are patentably distinct over the prior art cited by the Examiner, and that these claims are and were in full compliance with the requirements of 35 U.S.C. §112. The amendments to the claims, as presented herein, are not made for purposes of patentability within the meaning of 35 U.S.C. §§§§ 101, 102, 103 or 112. Rather, these amendments and additions are made simply for clarification and to round out the scope of protection to which Applicants are entitled.

**Objection to the Claims**

Claim 1 is objected to for encompassing non-elected embodiments. In response, Applicants note that claim 1 is a Markush-type generic claim in accordance with MPEP § 803.02, and recites a plurality of alternative APC surface molecules and Notch ligands.

Accordingly, Applicants request that the objection be reconsidered and withdrawn, as Markush-type generic claims can recite more than one elected species.

Claim 29 is objected to, because the Examiner contends that a conjugate is made by chemical conjugation and not by transforming a host cell. While Applicants do not agree that preparation of a conjugate necessarily involves chemical coupling, in the interest of expediting prosecution, Applicants note that claim 29 is amended to recite a “fusion protein” rather than a “conjugate,” and is dependent on instant claim 1, which is also directed to a fusion protein.

Accordingly, Applicants request that the objection be reconsidered and withdrawn.

## **II. THE REJECTIONS UNDER 35 U.S.C. 112 ARE OVERCOME**

### **Enablement**

Claims 1, 2, 29, and 31 were rejected under 35 U.S.C. 112, first paragraph, as allegedly failing to comply with the enablement requirement. This rejection is traversed.

Firstly, the Examiner alleged that there is a lack of in vivo working examples to show that the fragments of the Notch ligands recited in claim 1 retain signaling activity in vitro or in vivo. The Examiner further contended that a fragment can be as little as one amino acid, and that there is no disclosed correlation between the structure of the fragment and signaling activity.

In response, Applicants assert that the instant claims are enabled by the specification. Initially, Applicants also point out that, according to Section 2164.02 of the MPEP, “the specification need not contain an example if the invention is otherwise disclosed in such manner that one skilled in the art will be able to practice it without an undue amount of experimentation.” *In re Borkowski*, 422 F.2d 904, 908, 164 USPQ 642, 645 (CCPA 1970). In this case, the claimed invention is disclosed in such a manner that the skilled artisan can practice the invention, including the Notch ligands that retain signaling activity, without undue experimentation.

Applicants reiterate that the specification provides substantial guidance for the claimed invention. For instance, the components of the claimed fusion protein of claim 1 are described on page 3, lines 3-8, while the APC surface molecules recited in claim 1 are discussed on page 12, lines 17-19, and on page 13, lines 5-10. Notably, the specification describes polypeptides which can bind to MHC Class II molecules on page 39, line 18 – page 41, line 24. Further, the Notch ligand recited in claim 1 is disclosed on page 48, line 26 – page 50, line 49 of the

specification as originally filed, and on page 38, lines 25-30 in the specification as amended on June 28, 2004. In addition, the working examples demonstrate how to prepare a fusion protein comprising N-terminal 90 amino acids of TSST-1 and an N-terminal fragment of human Jagged1. Based on these teachings, one of ordinary skill in the art can prepare the scope of fusion proteins encompassed by the instant claims.

Applicants disagree with the Examiner's contention that there are no limitations on the Notch fragment and that it can be as little as one amino acid. Applicants submit that claim 1 clearly requires that the fragment comprises a Notch ligand DSL domain and at least one EGF-like repeat. These DSL and EGF domains are amply described in the specification, notably on pages 50-54. Hence, the skilled artisan can practice the claimed invention as it pertains to Notch ligands based on these disclosures in the specification. It is clear, for example, from pages 50-54 of the specification that the DSL domains and EGF repeats are substantially more than just one amino acid in length.

Applicants also assert that the specification provides guidance and direction for the correlation between the structure of the fragment and the signaling activity. As an example, Applicants refer to page 48, lines 12-25, and on pages 50-54.

The Examiner additionally alleged that there are no teachings of the structure of any variable domain of any antibody or binding fragment thereof for making and using the claimed conjugate, but conceded that amending claim 1 to recite "first sequence comprises an antibody or binding fragment thereof which binds to an antigen presenting cell (APC) surface molecule" would obviate this allegation. Applicants note that claim 1 is herein amended as noted by the Examiner, and express thanks to the Examiner for the suggestion.

Applicants further note that claim 29 is amended to recite a fusion protein rather than a conjugate, thereby obviating the rejection against claim 29.

For at least the reasons described herein, Applicants assert that instant claim 1, as well as claims 2, 29, and 31 which depend therefrom, are enabled by the specification. Accordingly, Applicants request reconsideration and withdrawal of the rejection under Section 112, first paragraph, pertaining to enablement.

#### **Written Description**

Claims 1, 2, 8, 29, and 31 were rejected under 35 U.S.C. 112, first paragraph, as allegedly failing to comply with the written requirement. This rejection is traversed.

The Examiner alleged that the specification does not reasonably provide a written description of any fragment of any Notch ligand retaining Notch signaling activity linked to or fused to any antibody or antibody fragment comprising just any variable that binds to any antigen presenting cell surface molecule for the claimed conjugate. The Examiner also contended that a fragment can be as little as one amino acid. Applicants respectfully disagree.

As discussed above, the specification provides an ample description of fragments of the invention. Applicants note that the fragment cannot be as little as one amino acid as asserted by the Examiner, because claim 1 requires the fragment to comprise a Notch ligand DSL domain and at least one EGF-like repeat, which are discussed in the specification on pages 50-54. Applicants also reiterate that correlation between the structure of the fragment and the signaling activity is discussed on page 48, lines 12-25, and on pages 50-54.

The Examiner contended that the specification does not describe the structure of any variable of any and all antibody or antibody fragment and still retains binding to APC surface molecule, but recommended amending claim 1 to recite “first sequence comprises an antibody or binding fragment thereof which binds to an antigen presenting cell (APC) surface molecule.” Applicants refer to the instance claim 1, which is amended according to the Examiner’s suggestion, thereby obviating this issue.

For at least the reasons described herein, Applicants assert that instant claim 1, as well as claims 2, 29, and 31 which depend therefrom, are enabled by the specification. Accordingly, Applicants request reconsideration and withdrawal of the rejection under Section 112, first paragraph, pertaining to written description.

#### **Indefiniteness**

Claims 29 was rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite. The Examiner contended that a “conjugate prepared by transforming a host cell” is ambiguous, and that preparation of a conjugate involves chemical coupling of proteins.

While Applicants do not agree that preparation of a conjugate necessarily involves chemical coupling, in the interest of expediting prosecution, Applicants refer to the instant claims, wherein instant claim 29 herein refers to a fusion protein. In addition, corresponding amendments have been made in the other claims.

Accordingly, Applicants request reconsideration and withdrawal of the rejection under Section 112, second paragraph.

**REQUEST FOR INTERVIEW**

If any issue remains as an impediment to allowance, an interview with the Examiner and her SPE are respectfully requested and the Examiner is additionally requested to contact the undersigned to arrange a mutually convenient time and manner for such an interview.

**CONCLUSION**

In view of the remarks and amendments herewith, the application is in condition for allowance. Favorable reconsideration of the application and prompt issuance of a Notice of Allowance are earnestly solicited. The undersigned looks forward to hearing favorably from the Examiner at an early date, and, the Examiner is invited to telephonically contact the undersigned to advance prosecution.

Respectfully submitted,

FROMMER LAWRENCE & HAUG LLP  
Attorneys for Applicants

By: *Russell A. Garman for Thomas J. Kowalski*  
Thomas J. Kowalski  
Reg. No. 32,147  
Russell A. Garman  
Reg. No. 62,419  
Tel: (212) 588-0800  
Fax: (212) 588-0500